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10/089,549

04/01/2002

Michio Kubota

KUBOTA=9

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05/02/2006

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EXAMINER

RAO, MANJUNATH N

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/089,549

Applicant(s)

KUBOTA ET AL.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 08 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3,48 and 52-54 is/are pending in the application.
- 4a) Of the above claim(s) 1,48 and 52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3,53 and 54 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

Claims 1, 3, 48, 52-54 are currently pending and are present for examination. Claims 3, 53-54 are now under consideration. Claims 1, 48, 52 remain withdrawn from consideration as being drawn to non-elected invention. Applicants have yet again amended the claims. However, Examiner appreciates applicant's efforts to remove all the confusion.

***Election/Restrictions***

Applicant's election with traverse of Group VII, which reads on Claims 3, 53-54 in Paper filed on 2-8-06 is acknowledged. The traversal is on the ground(s) that new claim 54 is a generic claim and that coexamination of all of Groups would not be undue burden on the Examiner. This is not found persuasive because while the searches for the groups may overlap, they are not coextensive and require independent searches. Furthermore, the claims are clearly drawn to enzymes with different structures and characteristics isolated from different sources even though they all may have similar function or activity. Therefore a search of all the claims will impose a serious burden on the Examiner. While applicants argue that new claim 54 is a generic claim reciting common features of the claimed enzyme, Examiner would have restricted differently if only applicants had presented the claim earlier. Presenting a generic claim after a restriction has been proposed does not remove the restriction. Therefore, Examiner will now examine the generic claim along with the elected group comprising claim 53.

The requirement is still deemed proper and is therefore made FINAL.

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Claims 1, 48, 52 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper filed on 2-8-06.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 54, 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 54 recites the phrase “which enzyme has a partial amino acid sequence of SEQ D NO:1...” in lines 9-10. It is not clear to the Examiner whether the claimed enzyme has a subsequence of SEQ ID NO:1, 11 or 18 or that the amino acid sequences SEQ D NO:1, 11 or 18 are indeed the partial sequence of the claimed enzymes. Examiner requests clarification.

Claim 54, 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 54 recites the phrase “said enzyme stabilized” in lines 11-12. It is not clear to the Examiner as to what applicants mean by the above phrase or which characteristic of the enzyme is stabilized. A perusal of the specification did not provide the Examiner with a specific definition. Examiner requests clarification.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54, 3, 53, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a native  $\alpha$ -isomaltosylglucosaccharide forming enzyme wherein said enzyme is specifically isolated from a wild type non-recombinant *B.globisporus* N75 deposited as FERM BP-7591, having the following characteristics such as a Molecular weight of about 136,000 + 20,000 Daltons on SDS-PAGE; an Isoelectric point of about 7.3 + 0.5 on isoelectrophoresis using ampholine; optimum temperature (i) About 50 degree C when incubated at a pH of 6 for 60 minutes; about 55 degree C when incubated at a pH of 6.0 for 60 minutes in the presence of 1 mM Ca ; an optimum pH about 6.0 when incubated at 35 degree C for 60 minutes; thermal stability (i) stable up to a temperature of about 45 degree C when incubated at a PH of 6.0 for 60 minutes; (ii) stable up to a temperature of about 50 degree C when incubated at a pH of 6.0 for 60 minutes in the presence of 1mM Ca ; pH stability Stable at pHs of about 5.0 to about 9.0 when incubated at 4 degree C for 24 hours and consisting of the amino acid sequences SEQ ID NO:1, 11 or 18 does not reasonably provide enablement for any such enzyme from any source including a recombinant *B.globisporus*, and having any physicochemical properties, and a partial amino acid sequence of SEQ ID NO:1, 11, or 18. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3)

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the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 54, 3, 53 are so broad as to encompass any  $\alpha$ -isomaltosylglucosaccharide forming enzymes from any source comprising partial amino acid sequence of SEQ ID NO:1, 11 or 18 and having any physicochemical properties including variants, mutants and recombinants. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of  $\alpha$ -isomaltosylglucosaccharide forming enzymes broadly encompassed by the claims including mutants, variants and recombinants. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a single native  $\alpha$ -isomaltosylglucosaccharide forming enzyme isolated from *B.globisporus* N75, FERM BP-7591 and consisting of amino acid sequence SEQ ID NO:1,11 or 18. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the use of the native enzyme isolated from *B.globisporus* N75, FERM BP-7591 as a  $\alpha$ -isomaltosylglucosaccharide forming enzyme but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed

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polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass  $\alpha$ -isomaltosylglucosaccharide forming enzymes from any or all sources including mutants, variants and recombinants because the specification does not establish: (A) regions of the protein structure which may be modified without affecting its specific activity; (B) the general tolerance of  $\alpha$ -isomaltosylglucosaccharide forming enzymes to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue in the amino acid sequence of the enzyme with an expectation of obtaining the desired biological

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function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including  $\alpha$ -isomaltosylglucosaccharide forming enzymes with an enormous number of amino acid modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)).

Without sufficient guidance, determination of  $\alpha$ -isomaltosylglucosaccharide forming enzymes having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 54, 3, 53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of polypeptides having  $\alpha$ -isomaltosylglucosaccharide forming activity and comprising one of the short amino acid sequences SEQ ID NO:1, 11 or 18. The specification does not contain any disclosure of the full structure of all the amino acids sequences included in the claimed genera. The genus of polypeptides claimed is a large variable genus with the potentiality of having many different structures. Therefore, many structurally distinct polypeptides are encompassed within the scope of these claims. The



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specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. A sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by amino acid sequence or a recitation of structural features common to members of the genus, **which features constitute a substantial portion of the genus**. The recited structural feature of the genus (i.e., partial amino acid sequences SEQ ID NO:1, 11 or 18) does not constitute a substantial portion of the genus as the remainder of the structure of the polypeptide having  $\alpha$ -isomaltosylglucosaccharide forming activity is completely undefined and the specification does not define the remaining structural features necessary for members of the genus to be selected. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at [www.uspto.gov](http://www.uspto.gov).

### ***Conclusion***

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura

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Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

A handwritten signature in black ink, appearing to read 'Manjunath N. Rao', with a stylized flourish at the end.

Manjunath N. Rao, Ph.D.  
Primary Examiner  
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April 27, 2006